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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/242,772	06/25/99	VAN DE VEN W	702-990278

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EXAMINER	
WILDER,C	
ART UNIT	**PAPER NUMBER**
1655	10

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/242,772	Applicant(s) Van De Ven, W. et al.
	Examiner CB Wilder	Group Art Unit 1655

☒ Responsive to communication(s) filed on *Mar 20, 2000*.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *28, 29, 32-34 (a)-(d), 35 and 47* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *28, 29, 32-34 (a)-(d), 35 and 47* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *6*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Priority

1. Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d). The certified copy has been filed in parent Application No. 09/242,772, filed on June 25, 1999.

Election/Restriction

2. Applicant's election without traverse of claims 26-33, cancellation of claims 27, 30 and 31, and substitution of claim 47 for claim 26 in Paper No. 9 is acknowledged. Since claim 33 drawn to a macromolecule is in included with Group I, the additional claims drawn to a macromolecule in Group II, claims 34 and 35 will be combined with Group I for prosecution. Only species drawn to a nucleic acid (a)-(d) in claim 34 which comprise the subject matter of Group I will be examined.

3. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventor ship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventor ship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(I).

Objections

4. The disclosure is objected to because of the following informalities:

(a) The specification and Figures contain sequences that are not identified by SEQ ID NOS:

Appropriate correction is required.

Claim Rejections - 35 USC § 101

5. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

6. Claims 28, 29, 32, 33, 34 (a)-(d), 35, and 47 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility. The claimed invention is drawn to an isolated nucleic acid wherein the nucleic acid is one of an oligonucleotide, a polynucleotide and a gene having a sequence of at least a part of the PLAG1 gene, sequence complementary thereto and degenerate sequences thereof. The invention is also drawn to an isolated nucleic acid having homology with the zinc finger domains of the PLAG1 gene in Figure 4A, or the complementary strand thereof, including modified, degenerate or elongated versions of both strands. The specification at page 2 defines the PLAG1 gene as a chromosome breakpoint gene and tumor aberrant growth gene. In Figure 4A of the specification, the applicant discloses the cDNA nucleotide sequence of the PLAG1 gene and discusses throughout the specification that the oligonucleotides or polynucleotides of the PLAG1 gene can be used as probes and primers to detect chromosomal aberrations associated with tumorigenesis. The specification continues at page 10 by stating that derivatives of the PLAG1 gene could be used in diagnosis and the preparation of therapeutical compositions, and in diagnosis and therapeutic treatment or in transgenic animal models for testing pharmaceutical for treatment of PLAG1-related malignant and

benign tumors. The specification however fails to discloses a specific asserted utility for the claimed isolated nucleic acid. The specification fails to discloses a specific asserted utility for the oligonucleotide or polynucleotide as probes and primers because the disclosed use of the oligonucleotide and polynucleotide is generally applicable to any nucleic acid and is therefore not particular to the isolated nucleic acid of the claimed invention. Since the specification sets forth no specific function of the PLAG1 gene, the claimed nucleic acid has no ascribed function. No direct connection is made between the claimed PLAG1 gene or any of the many tumor disease resulting in malignant or benign tumors, therefore, there is no apparent *indicia* of specificity to, for example to tumor growth. Furthermore, functionality of the nucleic acid and protein as subjected to insertions, deletions, substitutions, etc. is not demonstrated. Therefore, identifying and/or studying the claimed nucleotide sequence comprising a part of the PLAG1 gene does not define "a real world" context of use. The claimed probes and primers comprising a part of the PLAG1 gene are useful only for detecting a part of the PLAG1 gene. Because the claimed invention is not supported by a specific and substantial asserted utility for the reasons set forth above, one skilled in the art would not recognize a utility for the claimed invention.

Claims 28, 29, 32, 33, 34 (a)-(d), 35, and 47 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either an asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention because it cannot be determined from the specification whether the

nucleic acid sequence as claimed is indeed specific for the PLAG1 gene or for some other gene associated with tumorigenesis so that it would operate without undue experimentation.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 28, 29, 32, 33, 34 (a)-(d), 35, and 47 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the cDNA sequence of PLAG1 gene, it does not reasonably provide enablement for an isolated nucleic acid wherein the nucleic acid is one of an oligonucleotide, a polynucleotide and a gene having a sequence of at least a part of the PLAG1 gene and degenerate sequences thereof. The specification does not reasonably provide enablement for a nucleic acid having homology with the zinc finger domains of the PLAG1 gene, or the complementary strand thereof, including modified, degenerate or elongated versions of both strands. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with the claims. The first paragraph of section 112 requires the specification describe how to make and use the invention. There are many factors to be considered when determining whether there is sufficient evidence to support determination that a disclosure does not satisfy the enablement requirements and whether any

necessary experimentation is undue (See *In re Wands*, 858 F. 2d 731, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). These factor include, but are not limited to:

Quality of Experimentation Necessary:

The claimed invention is drawn to an isolated nucleic acid wherein the nucleic acid is one of an oligonucleotide, a polynucleotide and a gene having a sequence of at least a part of the PLAG1 gene sequences complementary thereto and degenerate sequence thereof. At page 4 of the specification, the applicant discloses that the PLAG1 gene is an oncogene and that aberrations in the gene usually leads to a benign tumor. At page 41 of the specification, the applicant discloses genomic organization of the PLAG1 gene including regulatory regions of the PLAG1 gene e.g. introns, exons, coding and non-coding regions. Although members of the PLAG gene family have been cloned and characterized in the prior art, the applicant fails to describe an isolated nucleic acid having a sequence comprising a part of the PLAG1 gene or gene comprising a part of the PLAG1 gene or degenerate sequences thereof. The specification does not discloses any of the various substitutions, insertions or deletions that are encompassed by the gene or degenerate sequences thereof. Additionally, the specification fails to provide information to enable one of ordinary skill in the art to make or used the claimed nucleic acid using the large number of undisclosed nucleotide variations encompassed by the claims. In the first Example, the applicant discloses directional chromosome walking studies wherein yeast artificial chromosome clones (YACs) are isolated and screen followed by methods of fluorescence *in situ* hybridization for chromosome mapping studies. In the second Example and subsequent Examples, the applicant discloses identification of a member of the PLAG gene family

using classical molecular biology techniques that are well known in the prior art. The Examples also discloses wherein probes and primers specific for the PLAG1 gene are utilized in methods of amplification and blotting to detect regions of the PLAG1 gene associated with tumor formation and growth. Nowhere in the Examples does the applicant provide information to enable one of ordinary skill in the art to isolate a nucleic acid comprising a part of the PLAG1 gene, or to isolate a gene comprising a sequence having a part of the PLAG 1 gene or any degenerate sequences thereof. As to the quality of experimentation required, one of skill in the art would have to design an experimental procedure to isolate a nucleic acid wherein the nucleic acid sequence is an oligonucleotide, a polynucleotide and a gene having a part of the PLAG1 gene and degenerate sequences thereof that is commensurate with the entire scope of the claims.

II. *Amount of Direction and Guidance*

The specification does not provide an isolated nucleic acid wherein the nucleic acid sequence is an oligonucleotide, a polynucleotide and a gene having at least part of the PLAG1 gene and a degenerate sequence thereof that bears a reasonable correlation to the entire scope of the claims. The examples starting at page 11 lack information concerning how to isolate any PLAG gene or how to isolate an oligonucleotide, polynucleotide, or gene comprising a part of the PLAG 1 gene or degenerate sequences thereof. The examples provided lack information concerning the size and composition of the nucleic acid sequence claimed to be associated with the PLAG 1 gene or information concerning nucleotide variations encompassed by the degenerate sequences thereof. Furthermore, it is not clear what algorithms or parameters have been used to identify homology

between the claimed nucleic acid sequence and the zinc finger domains of the PLAG1 gene, including modified, degenerate or elongated versions of both strands of the gene. Since the specification has not adequately identified the PLAG1 gene, it cannot be determined whether the claimed isolated nucleic acid sequence is indeed a sequence comprising a part of the PLAG1 gene or some other gene. Therefore, the claimed invention provides insufficient guidance and directions for one skilled in the art to make and use the claimed invention without undue experimentation.

III. Presence and Absence of Working Examples

The specification of the claim invention lacks proper working examples. starting at page 11, the specification discloses isolation and analysis of yeast artificial chromosome clones in chromsome walking studies. At page 32, the specification discloses general methods for identifying a member of the PLAG family in salivary glands. At page 53 and 54, the applicant disclose identification of a PLAG2 gene using classical molecular biology techniques. Beginning at page 56, the applicant discloses diagnostic test for pleomorphic adenomas of salivary glands using PLAG1-specific primers. At page 59, the applicant discloses using a PLAG2 gene as a diagnostic marker for chromosome anomalies. At page 60, the applicant discloses the use of animal models involving PLAG1 as tools in *in vivo* therapeutic drug testing. The Examples however fail to adequately disclose how to isolate the claimed nucleic acid sequence comprising at least a part of the PLAG1 gene or a gene having a sequence comprising a part of the PLAG1 gene or degenerate sequences thereof. Merely making reference to the PLAG1 gene, probes and primers of the PLAG1 gene or a PLAG2 gene as

a member of the PLAG1 family as being encompass in the invention does not enable the practitioner to reproduce the results as reported in the specification.

IV. Nature of the Invention

The nature of the invention is an isolated nucleic acid wherein the nucleic acid is one of an oligonucleotide, polynucleotide, and a gene having a sequence comprising at least a part of the PLAG1 gene and degenerate sequences thereof. The full scope of the claimed invention is not reproducible due to lack of guidance presented in the Examples beginning at page 11. As noted, the specification does not properly disclose an isolated nucleic acid as one of a gene having a sequence comprising at least a part of the PLAG1 gene or degenerate sequences thereof that bears a reasonable correlation to the entire scope of the claims.

V. Level of predictability and unpredictability in the art

The specification has not enabled an isolated nucleic acid wherein the nucleic acid is a gene having a sequence comprising a part of the PLAG1 gene or degenerate sequences thereof. Although certain relevant techniques useful to the claimed invention are known in the prior art, the prior art does not teach an isolated nucleic acid as set forth in the claimed invention.

Therefore, for all of the forgoing reasons, undue experimentation is necessary for one of skill in the art to obtain the claimed invention.

Claim Rejections - 35 USC § 112 first paragraph: Lack of adequate written description

9. Claims 28, 29, 32, 33, 34 (a)-(d), 35, and 47 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way

as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claimed invention is drawn to an isolated nucleic acid wherein the nucleic acid is one of an oligonucleotide, a polynucleotide and a gene having a sequence of at least a part of the PLAG1 gene, sequence complementary thereto and degenerate sequences thereof. In Figure 4A of the specification, the applicant discloses the cDNA nucleotide sequence of the PLAG1 gene and page 41 of the specification, the applicant discloses genomic organization of the PLAG1 gene including regulatory regions, i.e., introns, exons, coding and non-coding regions. The specification fails to describe an "isolated nucleic acid being a gene having a sequence comprising at least a part of the PLAG 1 gene or degenerate sequences thereof" which encompasses a large genus of genes and sequences that is not described or disclosed. Additionally, the specification fails to adequately described the various nucleotide variations, such as substitutions, insertions, deletions, nonsense or frameshift mutations that are encompassed by the gene and by the recitation of degenerate sequences thereof. Each of the claimed invention is a genus for which a representative number of species for each genus must be disclosed to meet the written description requirement of 112, first paragraph. As set forth by the Court in *Vas Cath Inc. V. Mahurkar*, 19 USPQ2d 1111, the written description must convey to one of skill in the art "with reasonable clarity" that as of the filing date applicant was in possession of the claimed invention. Absent a written description disclosing a representative number of the species of the isolated nucleic acid and macromolecule of claims 28, 29, 32, 33, 34 (a)-(d), 35, and 47 it has not been demonstrated

"with reasonable clarity" that applicant was, in fact, "in possession of the claimed invention" at the time the application for patent was filed.

Claim Rejections - 35 USC § 112

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claims 28, 29, rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(a) Claims 28 and 29 lack proper antecedent basis for "the complementary strand thereof". It is suggest changing "the" to "a".

(b) Claim 28, 29, 33, 34 (a)-(d), 35, and 47 are indefinite for "PLAG1 and "PLAG" because abbreviations often have more than one meaning. It is suggested amending the claim to recite the full name of the gene in claim 47.

(c) Claim 33 and 34 are indefinite for "CNNB1" because abbreviations often have more than one meaning. Additionally the use of the abbreviation "CNNB1" is not utilized in the specification. The specification recites "CTNNB1". It is suggested amending the claims to recite the full name of the gene in claim 33.

Claim Rejections - 35 USC § 102(b)

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> > (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

13. Claims 47 and 33 are rejected under 35 U.S.C. 102(b) as being anticipate by Kraus et al. (Genomics, 23, pages 272-274, December 1994). Claim 47 is broadly drawn to a nucleic acid in isolated form wherein the nucleic acid is one of an oligonucleotide, a polynucleotide and a gene having a sequence of at least a part of the PLAG 1 gene, sequences complementary thereof and degenerate sequences thereof. Kraus et al. discloses an isolated nucleotide sequence wherein the nucleic acid is an oligonucleotide and a polynucleotide fragment having a sequence of at least a part of a gene of the PLAG1 subfamily (page 272, column 2, last paragraph bridging column 1, page 273, lines 1-5, see also Figure legend 1.). Therefore, the claimed invention is anticipated by the reference of Kraus et al.

Claim 33 is drawn to a macromolecule comprising a nucleic acid in isolated form, comprising one of an oligonucleotide, a polynucleotide and a gene having a nucleotide sequence of at least a part of a T-gene selected from the group consisting of the PLAG1 subfamily of zinc finger protein genes, the CTNNB1 gene and fusion protein, or complementary degenerate versions of the nucleotide sequence. Kraus et al. discloses this embodiment (page 272, column 2, last paragraph bridging column 1, page 273, lines 1-5, see also Figure legend 1.)

Claim Rejections - 35 USC § 102

14. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

15. Claims 28 and 29 are rejected under 35 U.S.C. 102(a) as being anticipated by Kas et al. (July 24, 1996) Gene bank Accession No. U65002. Lab for Molecular Oncology. Cas Registry No. 186288-05-1). Claim 28 is drawn to an embodiment of claim 47, wherein the nucleic acid is homologous to the zinc finger domains of the PLAG1 gene the nucleotide sequence of which is depicted in figure 4A, or the complementary strand thereof, including modified, degenerate or elongated versions of both strands. Kas et al. discloses an isolated nucleic acid wherein the nucleic acid comprise a nucleotide sequence identical to the zinc finger domains of the PLAG1 nucleotide sequence of which is depicted in figure 4A (Genbank direct submission (GBN # U65002, entire sequence)). Therefore, the claimed invention is anticipated by the reference of Kas et al.

Claim 29 is drawn to an embodiment of claim 47 , wherein the nucleic acid comprise the nucleotide sequence of the PLAG1 gene as depicted in Figure 4A, or the complementary strand thereof, including modified, degenerate or elongated versions of both strands. Kas et al. discloses an isolated nucleic acid wherein the nucleic acid comprise a nucleotide sequence identical to the nucleotide sequence of the PLAG1 gene depicted in Figure 4A (Genbank direct submission (GBN

#U65002, entire sequence)). Therefore the claimed invention is anticipated by the reference of Kas et al.

16. Claims 47, 32, 33, 34 (a)-(d), and 35 are rejected under 35 U.S.C. 102(a) as being anticipated by Nollet et al. (Genomics March 1996). Regarding claim 47, Nollet discloses a nucleic acid in isolated form wherein the nucleic acid is an oligonucleotide and a polynucleotide fragment having a sequence of at least a part of a gene in the PLAG1 gene subfamily (page 414, "Materials and Method", lines 1-18 bridging top of column 2, lines 1-19). Therefore, the claimed invention is anticipated by the reference of Nollet et al.

Claim 32 and 35 are drawn to an embodiment of claim 4 7 and 33, wherein the nucleic acid or derivative is labeled. Nollet discloses this embodiment (Page 414, column 2, lines 25-26 and 59-60).

Claim 33 is drawn to a macromolecule comprising a derivative of a nucleic acid in isolated form, comprising one of an oligonucleotide, a polynucleotide, and a gene having a nucleotide sequence of at least a part of a T-gene selected from the group consisting of the PLAG subfamily of zinc finger proteins genes, the CTNNB1 gene and fusion thereof, or complementary or degenerate versions of the nucleotide sequence. Nollet discloses this embodiment (Page 418, bottom of column 1 bridging top of column 2, lines 1-24).

Claim 34 is drawn to an embodiment of claim 33, wherein the derivative is selected from the groups consisting of: (a) a transcript corresponding to the nucleic acid, (b) cDNA corresponding to the nucleic acid (c) sense or antisense DNA corresponding to the nucleic acid and (d) a nucleic acid

including a gene, or a derivative thereof, isolated by using at least a part of a gene as one of a probe or a primer. Nollet discloses a macromolecule wherein the derivative is a nucleic acid including a gene, or a derivative thereof, isolated by using at least a part of a T-gene as one of a probe or primer (page 414, "Materials and Method", lines 1-18 bridging top of column 2, lines 1-19).

Conclusion

17. No claims are allowed.

18. Any inquiry concerning this communication or earlier communications from the Exr. should be directed to Exr. Cynthia Wilder whose telephone number is (703) 305-1680. The Exr. can normally be reached on Monday through Thursday from 7:00 am to 5:00 pm.

If attempts to reach the Exr. by telephone are unsuccessful, the Exr.'s supervisor, W. Gary Jones, can be reached at (703) 308-1152. The official fax phone number for the Group is (703) 308-4242. The unofficial fax number is (703) 308-8724.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed the Group's receptionist whose telephone number is (703) 308-0196.

Cynthia B. Wilder, Ph.D.

May 16, 2000

STEPHANIE W. A. OWEN
PRIMARY EXAMINER